III. REMARKS

Claim Status

Claims 1, 3-15 and 17-22 remain active in the case.

Sequences

All disclosed sequences, e.g. all the sequences disclosed on pages 4, 5, 7, and 9 and in claims 4, 7, 15, and 17, are not listed in the Sequence Listing as required.

The examiner notes that the sequence disclosed in the specification and claims as SEQ ID NO: 3 is listed in the Sequence Listing as both SEQ ID NO: 3 and SEQ ID NO: 4; the sequence disclosed in the specification and claims as SEQ ID NO: 4 is listed in the Sequence Listing as SEQ ID NO: 5; and, the sequence disclosed in the specification and claims as SEQ ID NO: 5 is not listed in the Sequence Listing.

Appropriate correction has been made.

Applicants have provided a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, which includes each of the sequences disclosed in the specification as required by 37 CFR 1.821(c). A substitute copy of the "Sequence Listing" in computer readable form is provided as required by 37 CFR 1.821(e). Applicants have placed proper "SEQ ID NO:" identifiers for every appearance of sequences in the description or claims of the patent application.

Applicants have provided a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

Informalities

Grammatical, idiomatic, and spelling errors in the specification have been removed.

Claim Rejections – 35 U.S.C. § 112, first paragraph

The specification stands objected to and Claims 1, 3-11 and 17-22 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, in that the specification contains subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant traverses this ground for rejection.

The issue framed by the examiner is whether the disclosure describes and supports the ability of the peptides to elicit antibodies that bind singly, or in combination, and function for determination of all elastase isoforms in a body fluid sample.

The examiner states that applicant teaches only polyclonal antibodies to particular peptides and provides no description or guidance to any single antibody or monospecific species which functions in the invention to bind to all known elastase iso-enzymes that applicant has not described or enabled any antibody which functions **singly** as claimed; that applicant provides no guidance for usable combinations.

Applicant submits that it would be apparent to one skilled

in the art, once the problem was known and the solution conceived, to provide a specific combinstion of antibodies that would function as claimed in claim 1.

The examiner further states that some of the peptides suggested for use by applicant would be expected to elicit antibodies that bind to an isoform which corresponds to porcine elastase, which is not expressed in the human pancreas, and which would complicate the assay in certain patient populations.

Applicant respectfully disagrees.

The core point of present invention is that the claimed antibodies relate to specific sequences (SEQ ID NO: 2-16) of elastase isoforms which cannot be found in amylase sequences or elastases sequences of pigs or other animals (i.e. dogs, because Korean people eat dogs).

It is one of the important characteristics of the present invention that it leads to a highly specific test and prevents cross reactions and false results.

It is known that there is a homogenity about 80% between the amino acid sequences of elastases III A/III B and elastases II A/II B. Such a high homogenity also exists between the sequences of elastases III A/III B and amylases, lipases and chymotrypsin, in humans as well as in pigs.

The polyclonal antibodies of present invention are highly specific for epitopes of elastases III A/III B and elastases II A/II B, which exist only in these proteins. Cross reactions with other human pancreatic enzymes are demonstrably excluded as well as cross reactions with animal elastases,i.e. pig elastases. This is very important, because preparations of pig elastases are used for substitution in the treatment of patients with chronic

pancreatitis.

Claim Rejections - 35 U.S.C. 112, second paragraph

Claims 1, 3-15, and 17-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-5, and 20 involve method claims and, as such, they should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting, and detecting. "Employing" or "using" or similar terms are not valid method steps.

Applicant's active step is "administering".

In these claims, "the antigen" lacks antecedent basis. "Antigen" has been deleted from the claims.

In claim 3 and claims dependent thereupon, the examiner states it is not clear how antibodies are obtained "by means of antigens," e.g. it is not clear what applicant intends as encompassed because it is not clear if the antigens are immunogens, or binders in affinity chromatography, or used in some other means.

Applicant responds that the various procedures of raising antibodies to antigens are known to the art. Any conventional procedure can be utilized.

In claims 4, 7, 14, 15, and 17, and claims dependent thereupon, "SEQ ID NO:" identifiers are recited that do not correspond to sequences as listed in the Sequence Listing. This is easily corrected as required. The sequence ID numbers have been corrected.

In claim 6, the examiner states "the pancreas" lacks antecedent basis. Applicant suggests that the reference is to that of the patient and is supported by the text. It is not clear what applicant intends as excluded because the excluded amino acid sequence is of a peptide not an iso-enzyme. The claim has been amended to clarify the excluded sequence.

Claims 12-15 each fail to close the parentheses before the period. A period has been added to the amended claims.

In claim 17 and claims dependent thereupon, the examiner states "the antigen" lacks antecedent basis. Claim 17 has been amended to remove the reference to antigen.

The examiner states Claim 18 is indefinite in that the claim fails to further limit the subject matter of a previous claim and set forth an intended use but fail to point out what components are included or excluded by the claim language. Applicant submits that claim 18 limits claim 17 in that it requires two different antibodies and defines the test kit as an ELISA test kit.

In claim 19, the examiner states the interrelationships of the components are not clear, e.g. it is not clear if hemocyanin is a carrier substance. Applicant believes the function of the hemocyanin does not need to be specified.

In claim 20, the examiner states the interrelationships of the components are not clear, e.g. it is not clear if peptides are sub-units. It is not clear what is intended by "myeoloma cells" or "hybridoma cells which are cultivated in cell lines." Applicant traverses this rejection and believes the claim text is clear as it stands.

Claims 21 has been amended to correct the typographical

error.

Claim Rejections – 35 U.S.C. § 102 (b)

Claims 1, 3-8, 10-15, and 17-22 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Scheefers et al. (USP 5,622,837) in light of the instant disclosure for reasons of record.

Claims 1, 3-8, 10, 12-15, 17, 18, 21, and 22 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Sziegoleit et al. (Clin. Biochem. 22: 79, 1989) in light of the instant disclosure for reasons of record.

The fundamental distinction between applicant's invention and the disclosure of the references is that a diagnostic test using the polyclonal antibodies from Szigoleit and Scheefers would give false results, because the polyclonal antibodies derived from enzyme preparations of Szigoleit and of Scheefers are a large mixture of antibodies, which bind many different epitopes of elastases III A and III B. They also bind amylases, lipases, chymotrypsin and elastases from pigs or other animals. Therefore, the polyclonal antibodies from Szigoleit and Scheefers are not appropriate for the diagnostic of chronic pancreatitis.

The examiner voices a concern regarding applicant's point that elastase enzymes are digested in the intestinal tract. because the argument is contradictory to that which is known in the art and that which is disclosed in the specification, that elastase "displays extraordinary stability during the passage through the intestines".

Regarding the examiner's concern, applicant points out that elastase indeed has extraordinary stability, much more than amylase or chymotrypsin. But this doesn't mean that elastase is

not undergoing degradation at all. As a protein, of course it is digested, which is known by a person skilled in the art.

With regard to the opinion of the Examiner that the inventor had no possession of claimed invention, applicant submits the attached three publications of Dr. Weiss (Journal of Pediatric Gastroenterology and Nutrition P 58, page 19, Pancreatology page 21, Pancreas page 67, which show, that the claimed invention is already practically used and furthermore is advantageous over the prior art.

For the forgoing reasons, applicant believes the references do not explicitly or inherently read on applicant's claims. Favorable reconsideration is respectfully requested.

The Commissioner is hereby authorized to charge payment for any fees associated with this communication or credit any over payment to Deposit Account No. 14-1263.

Respectfully submitted,

NORRIS McLAUGHLIN & MARCUS, P.A.

By _____/Serle Ian Mosoff/_____
Serle Ian Mosoff
Attorney for Applicant(s)
Reg. No. 25,900

875 Third Avenue - 18th Floor
New York, New York 10022
Phone: (212) 808-0700
Fax: (212) 808-0844